

Appl. No. 09/724,571
Amdt. dated March 18, 2005
Reply to Office Action of December 10, 2004

PATENT

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1-77. (Canceled)

78. (Currently amended) A method of screening for compounds that inhibit A β production, comprising contacting a purified protein purified to apparent homogeneity comprising a segment of a β -secretase enzyme protein extending from residue 46 to residue 452 of SEQ ID NO:2 or up to several amino acids beyond, wherein the purified protein lacks a transmembrane region and residues 1-45 of SEQ ID NO:2, wherein (i) the segment lacks the signal sequence (amino acid residues 1-22 with respect to SEQ ID NO:2) and the putative pro region (amino acid residues 23-45 with respect to SEQ ID NO:2), and (ii) wherein the purified protein exhibits β -secretase activity, as evidenced by an ability to cleave a substrate selected from the group consisting of the 695 amino acid isotype of beta amyloid precursor protein (β -APP) between amino acids 596 and 597 thereof, MBP-C125wt and MBP-C125sw with (a) a test compound and (b) a β -secretase substrate, and selecting the test compound as capable of inhibiting beta-amyloid (A β) production if said protein exhibits less β -secretase activity in the presence of said compound than in the absence of said compound.

79. (Canceled)

80. (Canceled)

81. (Canceled)

82. (Canceled)

83. (Canceled)

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84. (Previously presented) The method of claim 78, wherein said β -secretase substrate is selected from the group consisting of MBP-C125wt, MBP-C125sw, APP, amyloid precursor protein (Swedish mutation) (β -APPsw), and β -secretase-cleavable fragments thereof.

85. (Previously presented) The method of claim 78, wherein said β -secretase substrate has a sequence selected from the group consisting of SEQ ID NO: 82, SEQ ID NO: 83, SEQ ID NO: 84, SEQ ID NO: 85, SEQ ID NO: 86, SEQ ID NO: 87, SEQ ID NO: 88, SEQ ID NO: 89, SEQ ID NO: 90, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 93, SEQ ID NO: 94, SEQ ID NO: 95, and SEQ ID NO: 96.

86-131. (Canceled)

132. (Withdrawn) The method of claim 78, wherein the β -secretase substrate has a sequence selected from the group consisting of SEQ ID NO: 72, SEQ ID NO: 78, and, SEQ ID NO: 81, and, SEQ ID NO: 97, and selecting the test compound as capable of inhibiting $A\beta$ production if said β -secretase polypeptide exhibits less β -secretase activity in the presence of the test compound than in the absence of the test compound.

133-135. (Canceled)